

Appendix 10. Stable coronary artery disease – Functional testing grouped

- Invasive coronary angiography – Functional testing grouped**
- Any revascularization – Functional testing grouped**
- Overall death – Functional testing grouped**
- Myocardial infarction – Functional testing grouped**
- Downstream testing – Functional testing grouped**

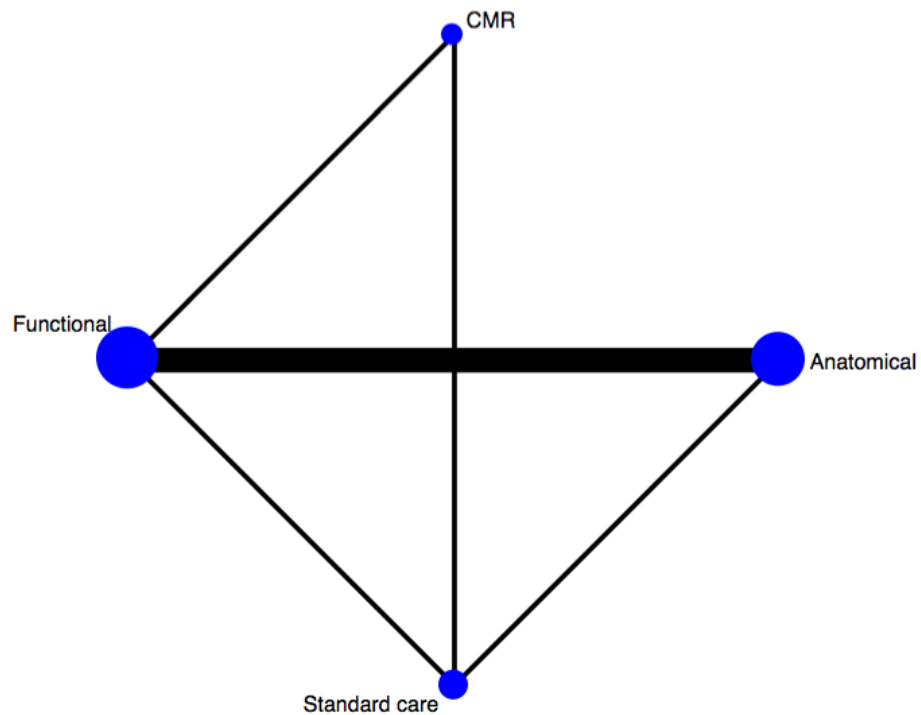
Invasive coronary angiography - Stable coronary artery disease - Functional testing grouped

Invasive coronary angiography – Functional testing grouped – Stable coronary artery disease – Pairwise meta-analysis results for the comparisons where at least 2 datasets were available.

Comparisons	Ref. D-RCT	No. Comparisons	OR (95%CI)	τ^2
Functional testing vs. Anatomical testing	R22 R24 R26 R27,R28 R30 R32	5	0.65 (0.58-0.74)	<0.001

Invasive coronary angiography – Functional testing grouped – Stable coronary artery disease – Network plot.

The size of nodes is proportional to the number of individuals randomized to each intervention and the thickness of lines to the number of direct comparisons in trials.

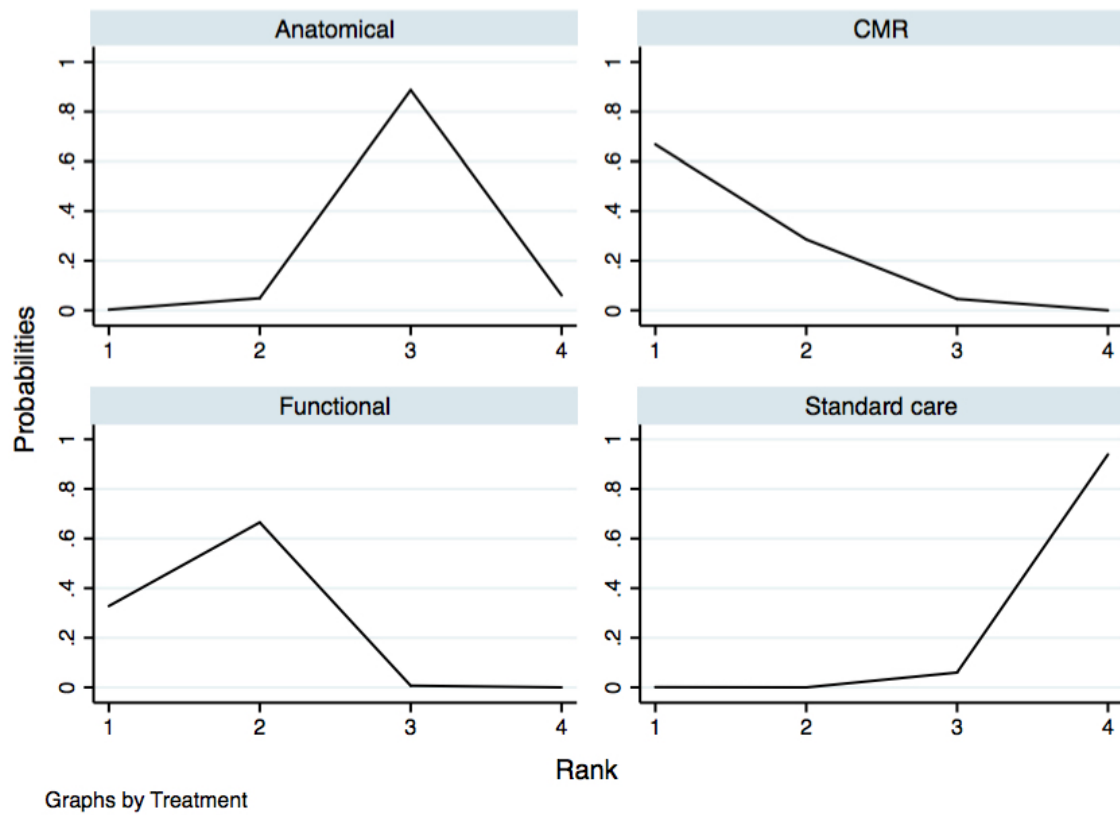


Invasive coronary angiography – Functional testing grouped – Stable coronary artery disease – League Table.

Estimates are odds ratios (OR). Ranges in parentheses are 95% CIs. Interventions are ordered according to efficacy ranking. Surface under the cumulative ranking curve values are given in the diagonal below each diagnostic strategy, with the probability of being the best treatment in parentheses. The larger the surface under the cumulative ranking curve value, the better the intervention. Heterogeneity $\tau^2 = 0.102$ (considered to be moderate heterogeneity). Statistical significant results are highlighted in bold.

CMR 87 (67)	1.14 (0.58-2.22)	1.80 (0.88-3.68)	2.71 (1.38-5.32)
0.88 (0.45-1.72)	Functional testing 77 (33)	1.58 (1.11-2.25)	2.39 (1.42-4.03)
0.56 (0.27-1.13)	0.63 (0.44-0.90)	Anatomical testing 33 (0)	1.51 (0.90-2.53)
0.37 (0.19-0.72)	0.42 (0.25-0.71)	0.66 (0.40-1.11)	Standard care 2 (0)

Invasive coronary angiography – Functional testing grouped – Stable coronary artery disease – Rankogram.



Invasive coronary angiography – Functional testing grouped – Stable coronary artery disease – Loop-specific heterogeneity estimates

Evaluation of inconsistency by using loop-specific heterogeneity estimates. From the above network we identified all closed loops of evidence and in each loop we investigated if direct and indirect evidence is in agreement. The overall p-value for the inconsistency model is $p < 0.001$.

Loop	IF	95%CI	p-value	Loop heterogeneity τ^2
Anatomical testing- Functional testing- Standard care	0.892	(0.48-1.31)	<0.001	<0.001

Invasive coronary angiography – Functional testing grouped – Stable coronary artery disease – Sidesplit approach for assessment of inconsistency (all p-values <0.05).

Comparison	Direct		Indirect		Difference		p-value
	Coefficient	SE	Coefficient	SE	Coefficient	SE	
Anatomical testing vs. Standard care	0.022	0.094	0.915	0.190	-0.892	0.212	<0.001
Anatomical testing vs. Functional testing	-0.425	0.062	-1.318	0.203	0.892	0.212	<0.001
CMR vs. Standard care	1.236	0.177	-0.548	0.379	1.784	0.424	<0.001
CMR vs. Functional testing	-0.103	0.172	1.681	0.385	-1.784	0.424	<0.001
Functional testing vs. Standard care	1.340	0.180	0.448	0.113	0.892	0.212	<0.001

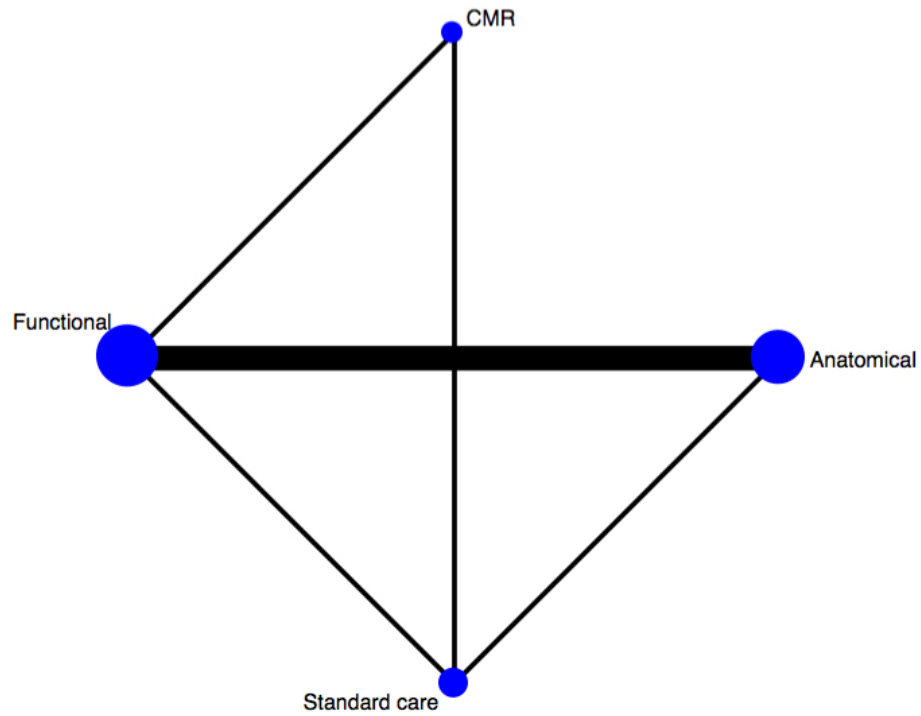
**Any revascularization - Stable coronary artery disease -
Functional testing grouped**

Any revascularization – Functional testing grouped – Stable coronary artery disease – Pairwise meta-analysis results for the comparisons where at least 2 datasets were available.

Comparisons	Ref. D-RCT	No. Comparisons	OR (95%CI)	τ^2
Functional testing vs. Anatomical testing	R22 R24 R26 R30 R32	5	0.55 (0.39-0.77)	0.049

Any revascularization – Functional testing grouped – Stable coronary artery disease – Network plot.

The size of nodes is proportional to the number of individuals randomized to each intervention and the thickness of lines to the number of direct comparisons in trials.

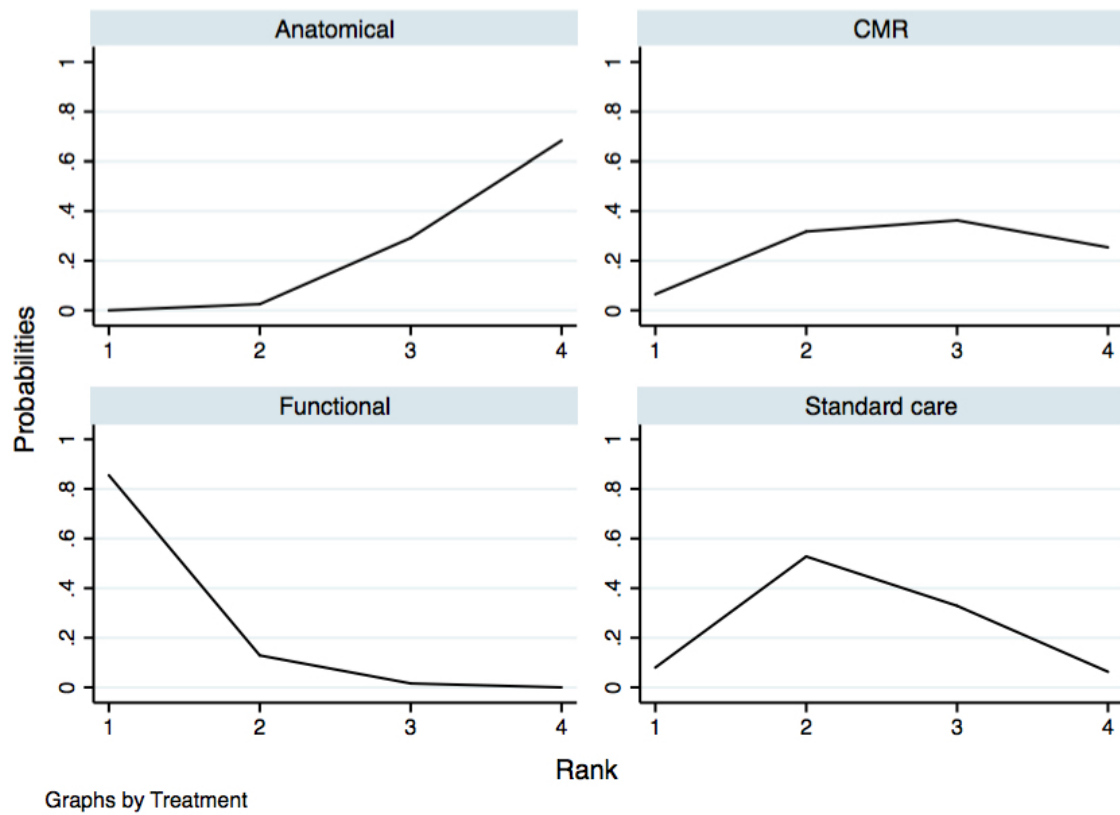


Any revascularization – Functional testing grouped – Stable coronary artery disease – League Table.

Estimates are odds ratios (OR). Ranges in parentheses are 95% CIs. Interventions are ordered according to efficacy ranking. Surface under the cumulative ranking curve values are given in the diagonal below each diagnostic strategy, with the probability of being the best treatment in parentheses. The larger the surface under the cumulative ranking curve value, the better the intervention. Heterogeneity $\tau^2 = 0.029$ (considered to be low heterogeneity). Statistical significant results are highlighted in bold.

Functional testing 95 (86)	1.37 (0.86-2.17)	1.47 (0.89-2.46)	1.76 (1.29-2.42)
0.73 (0.46-1.16)	Standard care 54 (8)	1.08 (0.61-1.91)	1.29 (0.91-1.84)
0.68 (0.41-1.13)	0.93 (0.52-1.64)	CMR 40 (7)	1.20 (0.69-2.07)
0.57 (0.41-0.78)	0.77 (0.54-1.10)	0.84 (0.48-1.44)	Anatomical testing 11 (0)

Any revascularization – Functional testing grouped – Stable coronary artery disease – Rankogram.



Any revascularization – Functional testing grouped – Stable coronary artery disease – Loop-specific heterogeneity estimates

Evaluation of inconsistency by using loop-specific heterogeneity estimates. From the above network we identified all closed loops of evidence and in each loop we investigated if direct and indirect evidence is in agreement. The overall p-value for the inconsistency model is p=0.15.

Loop	IF	95%CI	p-value	Loop heterogeneity τ^2
Anatomical testing- Functional testing- Standard care	0.381	(0.00-1.38)	0.456	0.050

Any revascularization – Functional testing grouped – Stable coronary artery disease – Sidesplit approach for assessment of inconsistency (all p-values >0.05).

Comparison	Direct		Indirect		Difference		p-value
	Coefficient	SE	Coefficient	SE	Coefficient	SE	
Anatomical testing vs. Standard care	-0.165	0.102	-0.620	0.296	0.455	0.313	0.147
Anatomical testing vs. Functional testing	-0.675	0.091	-0.221	0.300	-0.455	0.313	0.147
CMR vs. Standard care	-0.234	0.272	0.675	0.507	-0.909	0.626	0.147
CMR vs. Functional testing	-0.289	0.221	-1.120	0.576	0.909	0.626	0.147
Functional testing vs. Standard care	0.056	0.282	0.510	0.136	-0.455	0.313	0.147

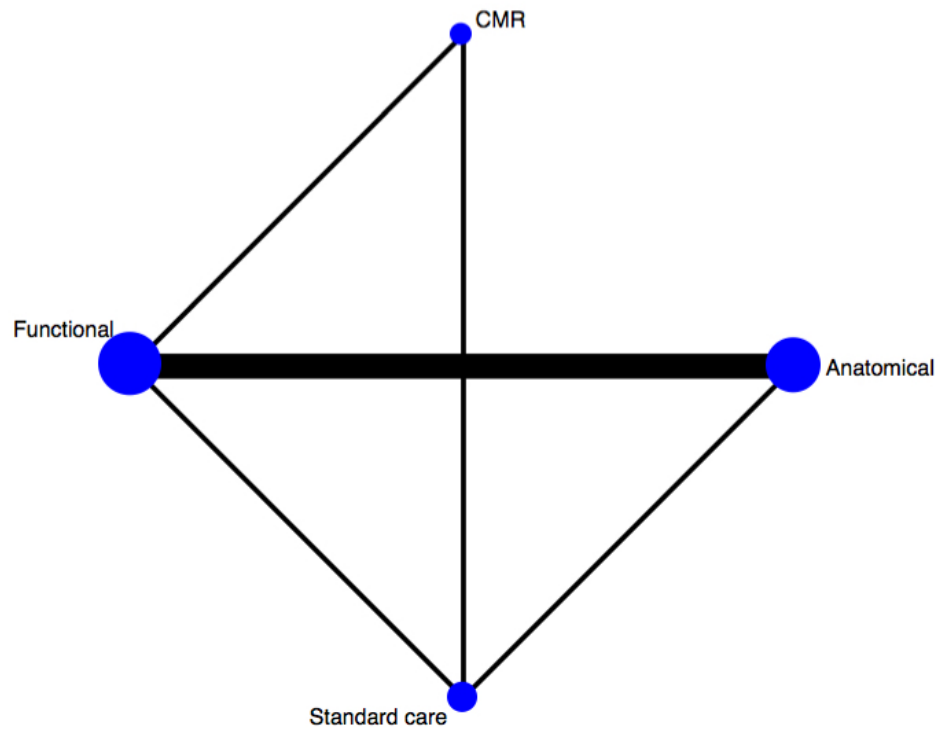
Overall death - Stable coronary artery disease - Functional testing group

Overall death – Functional testing grouped – Stable coronary artery disease – Pairwise meta-analysis results for the comparisons where at least 2 datasets were available.

Comparisons	Ref. D-RCT	No. Comparisons	OR (95%CI)	τ^2
Functional testing vs. Anatomical testing	R22 R24 R26 R30 R32	5	0.96 (0.73-1.27)	<0.001

Overall death – Functional testing grouped – Stable coronary artery disease – Network plot.

The size of nodes is proportional to the number of individuals randomized to each intervention and the thickness of lines to the number of direct comparisons in trials.

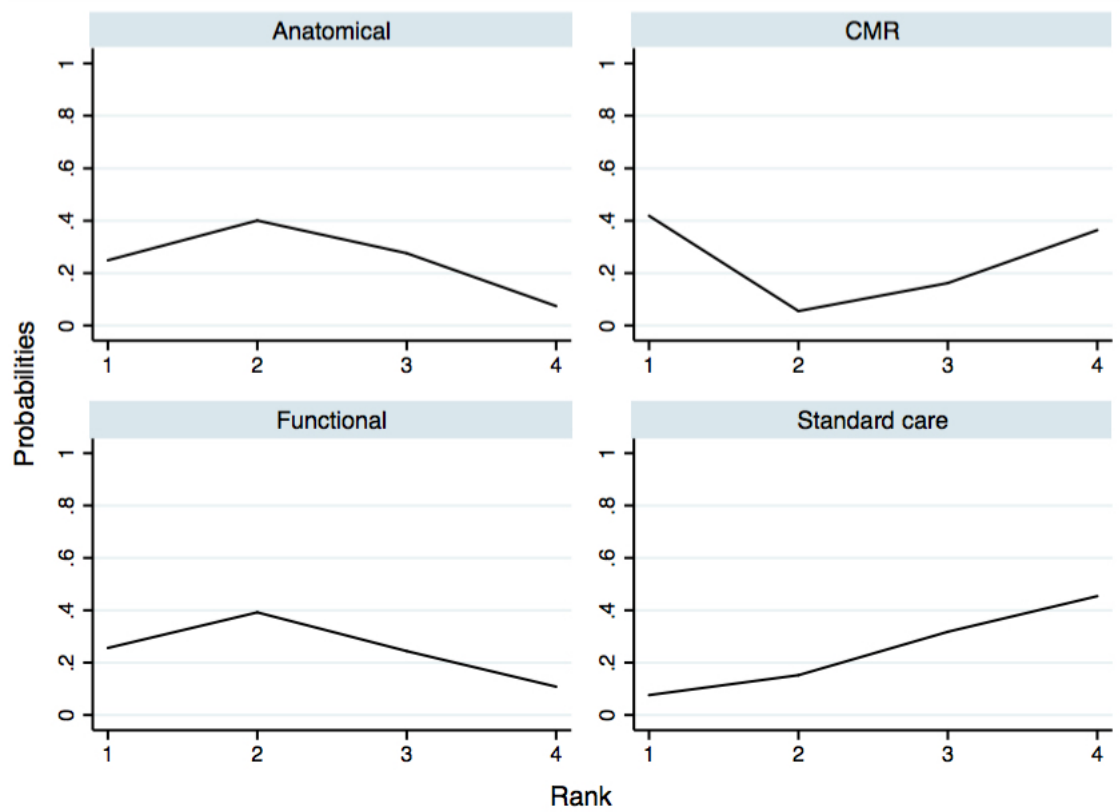


Overall death – Functional testing grouped – Stable coronary artery disease – League Table.

Estimates are odds ratios (OR). Ranges in parentheses are 95% CIs. Interventions are ordered according to efficacy ranking. Surface under the cumulative ranking curve values are given in the diagonal below each diagnostic strategy, with the probability of being the best treatment in parentheses. The larger the surface under the cumulative ranking curve value, the better the intervention. Heterogeneity $\tau^2 < 0.001$ (considered to be low heterogeneity). Statistical significant results are highlighted in bold.

Anatomical testing 61 (25)	0.99 (0.73-1.36)	1.06 (0.28-3.95)	1.27 (0.69-2.32)
1.01 (0.74-1.37)	Functional testing 60 (26)	1.06 (0.29-3.95)	1.28 (0.66-2.47)
0.95 (0.25-3.53)	0.94 (0.25-3.49)	CMR 51 (42)	1.20 (0.32-4.46)
0.79 (0.43-1.44)	0.78 (0.40-1.51)	0.83 (0.22-3.10)	Standard care 28 (8)

Overall death – Functional testing grouped – Stable coronary artery disease – Rankogram.



Overall death – Functional testing grouped – Stable coronary artery disease – Loop-specific heterogeneity estimates

Evaluation of inconsistency by using loop-specific heterogeneity estimates. From the above network we identified all closed loops of evidence and in each loop we investigated if direct and indirect evidence is in agreement. The overall p-value for the inconsistency model is p=0.34.

Loop	IF	95%CI	p-value	Loop heterogeneity τ^2
Anatomical testing- Functional testing- Standard care	0.548	(0.00-2.31)	0.542	<0.001

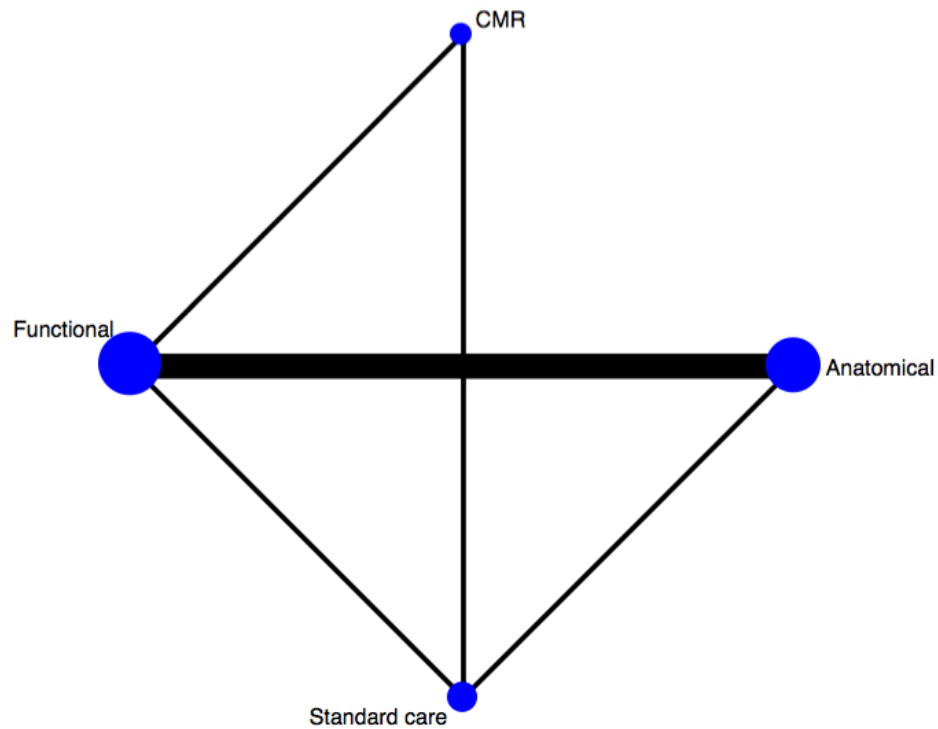
Myocardial infarction - Stable coronary artery disease – Functional testing group

Myocardial infarction – Functional testing grouped – Stable coronary artery disease – Pairwise meta-analysis results for the comparisons where at least 2 datasets were available.

Comparisons	Ref. D-RCT	No. Comparisons	OR (95%CI)	τ^2
Functional testing vs. Anatomical testing	R22 R24 R26 R30 R32	5	1.39 (0.89-2.17)	<0.001

Myocardial infarction – Functional testing grouped – Stable coronary artery disease – Network plot.

The size of nodes is proportional to the number of individuals randomized to each intervention and the thickness of lines to the number of direct comparisons in trials.

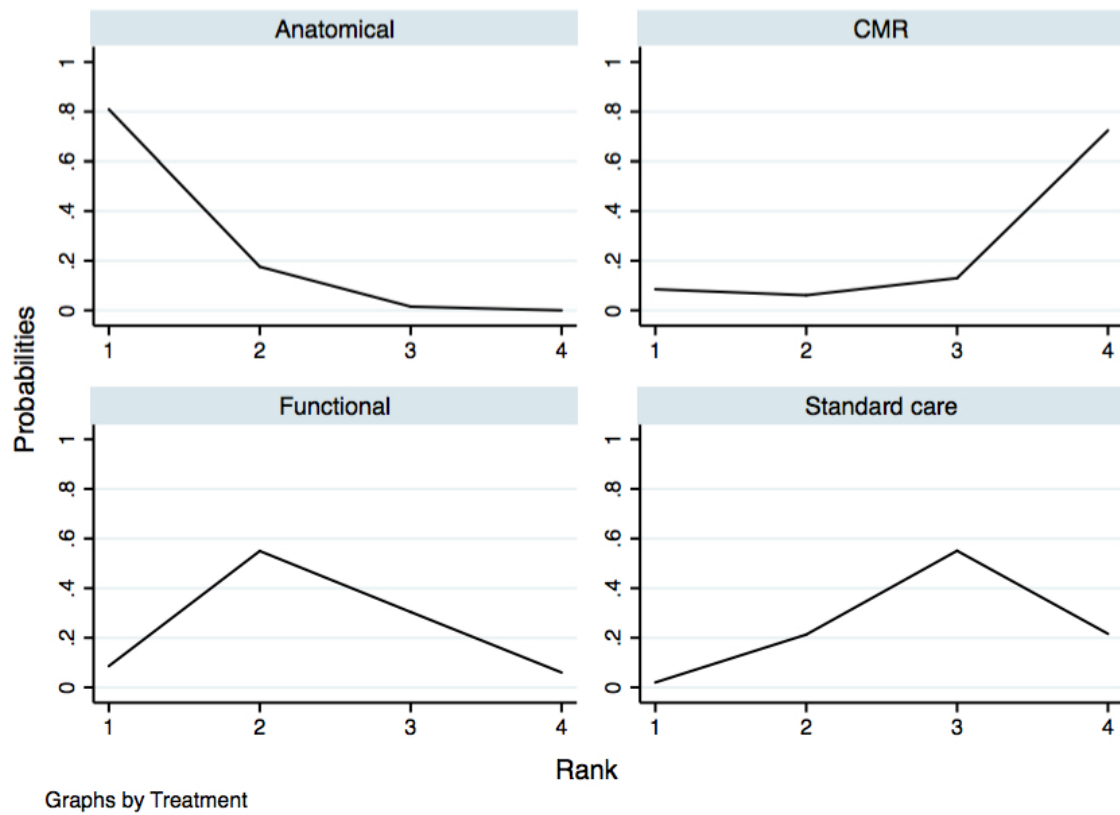


Myocardial infarction – Functional testing grouped – Stable coronary artery disease – League Table.

Estimates are odds ratios (OR). Ranges in parentheses are 95% CIs. Interventions are ordered according to efficacy ranking. Surface under the cumulative ranking curve values are given in the diagonal below each diagnostic strategy, with the probability of being the best treatment in parentheses. The larger the surface under the cumulative ranking curve value, the better the intervention. Heterogeneity $\tau^2 < 0.001$ (considered to be low heterogeneity). Statistical significant results are highlighted in bold.

Anatomical testing 93 (81)	1.35 (0.87-2.09)	1.66 (0.99-2.79)	2.66 (0.68-10.41)
0.74 (0.48-1.15)	Functional testing 55 (9)	1.23 (0.64-2.38)	1.97 (0.50-7.67)
0.60 (0.36-1.01)	0.81 (0.42-1.57)	Standard care 35 (2)	1.60 (0.41-6.24)
0.38 (0.10-1.47)	0.51 (0.13-1.98)	0.62 (0.16-2.44)	CMR 17 (9)

Myocardial infarction – Functional testing grouped – Stable coronary artery disease – Rankogram.



Myocardial infarction – Functional testing grouped – Stable coronary artery disease – Loop-specific heterogeneity estimates

Evaluation of inconsistency by using loop-specific heterogeneity estimates. From the above network we identified all closed loops of evidence and in each loop we investigated if direct and indirect evidence is in agreement. The overall p-value for the inconsistency model is p=0.60.

Loop	IF	95%CI	p-value	Loop heterogeneity τ^2
Anatomical testing- Functional testing- Standard care	0.555	(0.00-2.64)	0.602	<0.001

Myocardial infarction – Functional testing grouped – Stable coronary artery disease – Sidesplit approach for assessment of inconsistency (all p-values >0.05).

Comparison	Direct		Indirect		Difference		p-value
	Coefficient	SE	Coefficient	SE	Coefficient	SE	
Anatomical testing vs. Standard care	0.471	0.274	1.026	1.029	-0.555	1.065	0.602
Anatomical testing vs. Functional testing	0.326	0.229	-0.229	1.040	0.555	1.065	0.602
CMR vs. Standard care	-0.223	0.840	-1.333	1.796	1.110	2.129	0.602
CMR vs. Functional testing	-0.923	0.839	0.188	1.797	-1.110	2.129	0.602
Functional testing vs. Standard care	0.699	1.003	0.144	0.357	0.555	1.065	0.602

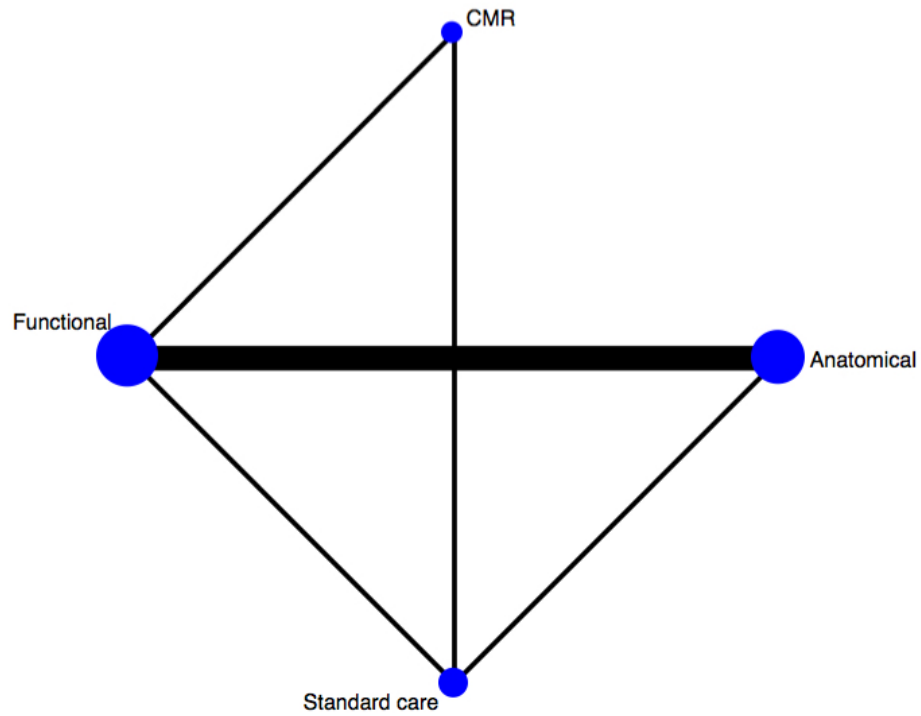
Downstream testing - Functional testing group -
Stable coronary artery disease

Downstream testing – Functional testing grouped – Stable coronary artery disease – Pairwise meta-analysis results for the comparisons where at least 2 datasets were available.

Comparisons	Ref. D-RCT	No. Comparisons	OR (95%CI)	τ^2
Functional testing vs. Anatomical testing	R22 R24 R26 R30 R32	5	1.27 (0.61-2.64)	0.637

Downstream testing – Functional testing grouped – Stable coronary artery disease – Network plot.

The size of nodes is proportional to the number of individuals randomized to each intervention and the thickness of lines to the number of direct comparisons in trials.

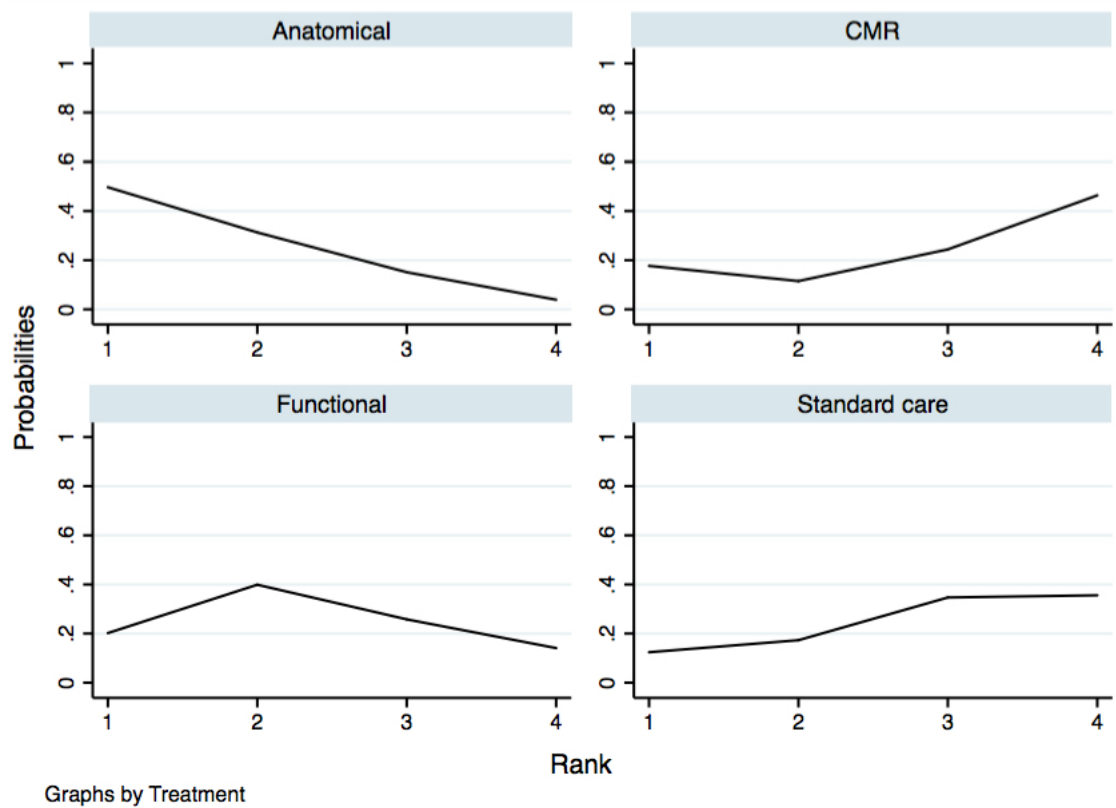


Downstream testing – Functional testing grouped – Stable coronary artery disease – League Table.

Estimates are odds ratios (OR). Ranges in parentheses are 95% CIs. Interventions are ordered according to efficacy ranking. Surface under the cumulative ranking curve values are given in the diagonal below each diagnostic strategy, with the probability of being the best treatment in parentheses. The larger the surface under the cumulative ranking curve value, the better the intervention. Heterogeneity $\tau^2 = 0.578$ (considered to be high heterogeneity). Statistical significant results are highlighted in bold.

Anatomical testing 76 (50)	1.18 (0.61-2.29)	1.56 (0.51-4.81)	1.63 (0.35-7.48)
0.85 (0.44-1.65)	Functional testing 55 (20)	1.33 (0.43-4.13)	1.38 (0.32-5.93)
0.64 (0.21-1.98)	0.75 (0.24-2.35)	Standard care 36 (12)	1.04 (0.24-4.49)
0.61 (0.13-2.83)	0.72 (0.17-3.10)	0.96 (0.22-4.13)	CMR 34 (18)

Downstream testing – Functional testing grouped – Stable coronary artery disease – Rankogram.



Downstream testing – Functional testing grouped – Stable coronary artery disease – Loop-specific heterogeneity estimates

Evaluation of inconsistency by using loop-specific heterogeneity estimates. From the above network we identified all closed loops of evidence and in each loop we investigated if direct and indirect evidence is in agreement. The overall p-value for the inconsistency model is p=0.53.

Loop	IF	95%CI	p-value	Loop heterogeneity τ^2
Anatomical testing- Functional testing- Standard care	0.784	(0.00-3.20)	0.525	0.637

Downstream testing – Functional testing grouped – Stable coronary artery disease – Sidesplit approach for assessment of inconsistency (all p-values >0.05).

Comparison	Direct		Indirect		Difference		p-value
	Coefficient	SE	Coefficient	SE	Coefficient	SE	
Anatomical testing vs. Standard care	0.109	0.814	0.892	0.936	-0.783	1.240	0.528
Anatomical testing vs. Functional testing	0.236	0.380	-0.548	1.181	0.784	1.241	0.528
CMR vs. Standard care	0.147	0.849	-1.420	2.324	1.568	2.481	0.528
CMR vs. Functional testing	-0.509	0.845	1.058	2.328	-1.568	2.481	0.528
Functional testing vs. Standard care	0.657	0.855	-0.127	0.898	0.784	1.241	0.528